

GGA TCC GGC TCC GGA ACG GAT TAC ACT CTG 300
Gly Ser Gly Ser Gly Thr Asp Tyr Thr Leu
70 75

ACC ATC AGC AGT CTG CAA CCT GAG GAC TTC 330
Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
80 85

GCT ACG TAT TAC TGT CAG AAC GTT TTA AAT 360
Ala Thr Tyr Tyr Cys Gln Asn Val Leu Asn
90 95

ACT CCG TTG ACT TTC GGA CAG GGT ACC AAG 390
Thr Pro Leu Thr Phe Gly Gln Gly Thr Lys
100 105

GTG GAA ATA AAA CGA ACT GTG GCT GCA CCA 420
Val Glu Ile Lys Arg Thr Val Ala Ala Pro
110 115

TCT GTC TTC ATC TTC CCG CCA TCT GAT GAG 450
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
120 125

CAG TTG AAA TCT GGA ACT GCC TCT GTT GTG 480
Gln Leu Lys Ser Gly Thr Ala Ser Val Val
130 135

TGC CTG CTG AAT AAC TTC TAT CCC AGA GAG 510
Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
140 145

GCC AAA GTA CAG TGG AAG GTG GAT AAC GCC 540
Ala Lys Val Gln Trp Lys Val Asp Asn Ala
150 155

CTC CAA TCG GGT AAC TCC CAG GAG AGT GTC 570
Leu Gln Ser Gly Asn Ser Gln Glu Ser Val
160 165

ACA GAG CAG GAC AGC AAG GAC AGC ACC TAC 600
Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
170 175

AGC CTC AGC AGC ACC CTG ACG CTG AGC AAA 630
Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
180 185

GCA GAC TAC GAG AAA CAC AAA GTC TAC GCC 660
Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
190 195

TGC GAA GTC ACC CAT CAG GGC CTG AGC TCG 690
Cys Glu Val Thr His Gln Gly Leu Ser Ser
200 205

CCC GTC ACA AAG AGC TTC AAC AGG GGA GAG 720
Pro Val Thr Lys Ser Phe Asn Arg Gly Glu
210 215

TGT TAG 726
Cys

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 726 base pairs
- (B) TYPE: Nucleic Acid
- (C) STRANDEDNESS: Double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: Other nucleic acid

- (A) DESCRIPTION: 5G1.1 VL +KLV56B
(Humanized light chain)

2189015

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

ATG GGA ATC CAA GGA GGG TCT GTC CTG TTC 30

Met Gly Ile Gln Gly Gly Ser Val Leu Phe

-25 -20

GGG CTG CTG CTC GTC CTG GCT GTC TTC TGC 60

Gly Leu Leu Leu Val Leu Ala Val Phe Cys

-15 -10

CAT TCA GGT CAT AGC CTG CAG GAT ATC CAG 90

His Ser Gly His Ser Leu Gln Asp Ile Gln

-5 1 5

ATG ACC CAG TCC CCG TCC TCC CTG TCC GCC 120

Met Thr Gln Ser Pro Ser Ser Leu Ser Ala

10 15

TCT GTG GGC GAT AGG GTC ACC ATC ACC TGC 150

Ser Val Gly Asp Arg Val Thr Ile Thr Cys

20 25

GGC GCC AGC GAA AAC ATC TAT GGC GCG CTG 180

Gly Ala Ser Glu Asn Ile Tyr Gly Ala Leu

30 35

AAC TGG TAT CAA CGT AAA CCT GGG AAA GCT 210

Asn Trp Tyr Gln Arg Lys Pro Gly Lys Ala

40 45

CCG AAG CTT CTG ATT TAC GGT GCG ACG AAC 240

Pro Lys Leu Leu Ile Tyr Gly Ala Thr Asn

50 55

CTG GCA GAT GGA GTC CCT TCT CGC TTC TCT 270

Leu Ala Asp Gly Val Pro Ser Arg Phe Ser

60 65

WO 95/29697

2189015

PCT/US95/05688

- 130 -

GGA TCC GGC TCC GGA ACG GAT TTC ACT CTG 300
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
70 75

ACC ATC AGC AGT CTG CAG CCT GAA GAC TTC 330
Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe
80 85

GCT ACG TAT TAC TGT CAG AAC GTT TTA AAT 360
Ala Thr Tyr Tyr Cys Gln Asn Val Leu Asn
90 95

ACT CCG TTG ACT TTC GGA CAG GGT ACC AAG 390
Thr Pro Leu Thr Phe Gly Gln Gly Thr Lys
100 105

GTG GAA ATA AAA CGA ACT GTG GCT GCA CCA 420
Val Glu Ile Lys Arg Thr Val Ala Ala Pro
110 115

TCT GTC TTC ATC TTC CCG CCA TCT GAT GAG 450
Ser Val Phe Ile Phe Pro Pro Ser Asp Glu
120 125

CAG TTG AAA TCT GGA ACT GCC TCT GTT GTG 480
Gln Leu Lys Ser Gly Thr Ala Ser Val Val
130 135

TGC CTG CTG AAT AAC TTC TAT CCC AGA GAG 510
Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
140 145

GCC AAA GTA CAG TGG AAG GTG GAT AAC GCC 540
Ala Lys Val Gln Trp Lys Val Asp Asn Ala
150 155

2189015

CTC CAA TCG GGT AAC TCC CAG GAG AGT GTC 570
Leu Gln Ser Gly Asn Ser Gln Glu Ser Val
160 165

ACA GAG CAG GAC AGC AAG GAC AGC ACC TAC 600
Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr
170 175

AGC CTC AGC AGC ACC CTG ACG CTG AGC AAA 630
Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys
180 185

GCA GAC TAC GAG AAA CAC AAA GTC TAC GCC 660
Ala Asp Tyr Glu Lys His Lys Val Tyr Ala
190 195

TGC GAA GTC ACC CAT CAG GGC CTG AGC TCG 690
Cys Glu Val Thr His Gln Gly Leu Ser Ser
200 205

CCC GTC ACA AAG AGC TTC AAC AGG GGA GAG 720
Pro Val Thr Lys Ser Phe Asn Arg Gly Glu
210 215

TGT TAG 726
Cys

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 711 base pairs
- (B) TYPE: Nucleic Acid
- (C) STRANDEDNESS: Double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: Other nucleic acid

- (A) DESCRIPTION: 5G1.1 VL + 012
(Humanized light chain)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

ATG GAC ATG AGG GTC CCC GCT CAG CTC CTG 30
Met Asp Met Arg Val Pro Ala Gln Leu Leu
-20 -15

GGG CTC CTG CTA CTC TGG CTC CGA GGT GCC 60
Gly Leu Leu Leu Leu Trp Leu Arg Gly Ala
-10 -5

AGA TGT GAT ATC CAG ATG ACC CAG TCC CCG 90
Arg Cys Asp Ile Gln Met Thr Gln Ser Pro
1 5

TCC TCC CTG TCC GCC TCT GTG GGC GAT AGG 120
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
10 15

GTC ACC ATC ACC TGC GGC GCC AGC GAA AAC 150
Val Thr Ile Thr Cys Gly Ala Ser Glu Asn
20 25

ATC TAT GGC GCG CTG AAC TGG TAT CAA CAG 180
Ile Tyr Gly Ala Leu Asn Trp Tyr Gln Gln
30 35

AAA CCC GGG AAA GCT CCG AAG CTT CTG ATT 210
Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
40 45

TAC GGT GCG ACG AAC CTG GCA GAT GGA GTC 240
Tyr Gly Ala Thr Asn Leu Ala Asp Gly Val
50 55

CCT TCT CGC TTC TCT GGA TCC GGC TCC GGA 270
Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
60 65

2189015

ACG GAT TTC ACT CTG ACC ATC AGC AGT CTG 300
Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu
70 75

CAG CCT GAA GAC TTC GCT ACG TAT TAC TGT 330
Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
80 85

CAG AAC GTT TTA AAT ACT CCG TTG ACT TTC 360
Gln Asn Val Leu Asn Thr Pro Leu Thr Phe
90 95

GGA CAG GGT ACC AAG GTG GAA ATA AAA CGA 390
Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
100 105

ACT GTG GCT GCA CCA TCT GTC TTC ATC TTC 420
Thr Val Ala Ala Pro Ser Val Phe Ile Phe
110 115

CCG CCA TCT GAT GAG CAG TTG AAA TCT GGA 450
Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly
120 125

ACT GCC TCT GTT GTG TGC CTG CTG AAT AAC 480
Thr Ala Ser Val Val Cys Leu Leu Asn Asn
130 135

TTC TAT CCC AGA GAG GCC AAA GTA CAG TGG 510
Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp
140 145

AAG GTG GAT AAC GCC CTC CAA TCG GGT AAC 540
Lys Val Asp Asn Ala Leu Gln Ser Gly Asn
150 155

- 134 -

TCC CAG GAG AGT GTC ACA GAG CAG GAC AGC 570
Ser Gln Glu Ser Val Thr Glu Gln Asp Ser
160 165

AAG GAC AGC ACC TAC AGC CTC AGC AGC ACC 600
Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr
170 175

CTG ACG CTG AGC AAA GCA GAC TAC GAG AAA 630
Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys
180 185

CAC AAA GTC TAC GCC TGC GAA GTC ACC CAT 660
His Lys Val Tyr Ala Cys Glu Val Thr His
190 195

CAG GGC CTG AGC TCG CCC GTC ACA AAG AGC 690
Gln Gly Leu Ser Ser Pro Val Thr Lys Ser
200 205

TTC AAC AGG GGA GAG TGT TAG 711
Phe Asn Arg Gly Glu Cys
210

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 750 base pairs
- (B) TYPE: Nucleic Acid
- (C) STRANDEDNESS: Double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: Other nucleic acid

- (A) DESCRIPTION: 5G1.1 VH + IGHRD
(Humanized Fd)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

ATG AAG TGG AGC TGG GTT ATT CTC TTC CTC 30
Met Lys Trp Ser Trp Val Ile Leu Phe Leu

-15

-10

CTG TCA GTA ACT GCC GGC GTC CAC TCC CAA 60
Leu Ser Val Thr Ala Gly Val His Ser Gln

-5

1

GTC CAA CTG GTG CAA TCC GGC GCC GAG GTC 90
Val Gln Leu Val Gln Ser Gly Ala Glu Val

5

10

AAG AAG CCA GGG GCC TCA GTC AAA GTG TCC 120
Lys Lys Pro Gly Ala Ser Val Lys Val Ser

15

20

TGT AAA GCT AGC GGC TAT ATT TTT TCT AAT 150
Cys Lys Ala Ser Gly Tyr Ile Phe Ser Asn

25

30

TAT TGG ATT CAA TGG GTG CGT CAG GCC CCC 180
Tyr Trp Ile Gln Trp Val Arg Gln Ala Pro

35

40

GGG CAG GGC CTG GAA TGG ATG GGT GAG ATC 210
Gly Gln Gly Leu Glu Trp Met Gly Glu Ile

45

50

TTA CCG GGC TCT GGT AGC ACC GAA TAT GCC 240
Leu Pro Gly Ser Gly Ser Thr Glu Tyr Ala

55

60

CAA AAA TTC CAG GGC CGT GTT ACT ATG ACT 270
Gln Lys Phe Gln Gly Arg Val Thr Met Thr

65

70

WO 95/29697

2189015

PCT/US95/05688

- 136.-

CGT GAC ACT TCG ACT AGT ACA GTA TAC ATG 300
Arg Asp Thr Ser Thr Ser Thr Val Tyr Met
75 80

GAG CTC TCC AGC CTG CGA TCG GAG GAC ACG 330
Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr
85 90

GCC GTC TAT TAT TGC GCG CGT TAT TTT TTT 360
Ala Val Tyr Tyr Cys Ala Arg Tyr Phe Phe
95 100

GGT TCT AGC CCG AAT TGG TAT TTT GAT GTT 390
Gly Ser Ser Pro Asn Trp Tyr Phe Asp Val
105 110

TGG GGT CAA GGA ACC CTG GTC ACT GTC TCG 420
Trp Gly Gln Gly Thr Leu Val Thr Val Ser
115 120

AGC GCC TCC ACC AAG GGC CCA TCG GTC TTC 450
Ser Ala Ser Thr Lys Gly Pro Ser Val Phe
125 130

CCC CTG GCG CCC TCC TCC AAG AGC ACC TCT 480
Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser
135 140

GGG GGC ACA GCG GCC CTG GGC TGC CTG GTC 510
Gly Gly Thr Ala Ala Leu Gly Cys Leu Val
145 150

AAG GAC TAC TTC CCC GAA CCG GTG ACG GTG 540
Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
155 160

- 137 -

2189015

TCG TGG AAC TCA GGC GCC CTG ACC AGC GGC 570
Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly
165 170

GTG CAC ACC TTC CCG GCT GTC CTA CAG TCC 600
Val His Thr Phe Pro Ala Val Leu Gln Ser
175 180

TCA GGA CTC TAC TCC CTC AGC AGC GTG GTG 630
Ser Gly Leu Tyr Ser Leu Ser Ser Val Val
185 190

ACC GTG CCC TCC AGC AGC TTG GGC ACC CAG 660
Thr Val Pro Ser Ser Ser Leu Gly Thr Gln
195 200

ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC 690
Thr Tyr Ile Cys Asn Val Asn His Lys Pro
205 210

AGC AAC ACC AAG GTG GAC AAG AAA GTT GAG 720
Ser Asn Thr Lys Val Asp Lys Lys Val Glu
215 220

CCC AAA TCT TGT GAC AAA ACT CAC ACA TAA 750
Pro Lys Ser Cys Asp Lys Thr His Thr
225 230

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 747 base pairs
- (B) TYPE: Nucleic Acid
- (C) STRANDEDNESS: Double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: Other nucleic acid

WO 95/29697

2189015

PCT/US95/05688

- 138. -

(A) DESCRIPTION: 5G1.1 scFv.D012
(Humanized scFv)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

ATG GCC GAT ATC CAG ATG ACC CAG TCC CCG 30
Met Ala Asp Ile Gln Met Thr Gln Ser Pro
1 5 10

TCC TCC CTG TCC GCC TCT GTG GGC GAT AGG 60
Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
15 20

GTC ACC ATC ACC TGC GGC GCC AGC GAA AAC 90
Val Thr Ile Thr Cys Gly Ala Ser Glu Asn
25 30

ATC TAT GGC GCG CTG AAC TGG TAT CAA CAG 120
Ile Tyr Gly Ala Leu Asn Trp Tyr Gln Gln
35 40

AAA CCT GGG AAA GCT CCG AAG CTT CTG ATT 150
Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
45 50

TAC GGT GCG ACG AAC CTG GCA GAT GGA GTC 180
Tyr Gly Ala Thr Asn Leu Ala Asp Gly Val
55 60

CCT TCT CGC TTC TCT GGA TCC GGC TCC GGA 210
Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly
65 70

ACG GAT TTC ACT CTG ACC ATC ACC AGT CTG 240
Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu
75 80

2189015

- 139 -

CAG CCT GAA GAC TTC GCT ACG TAT TAC TGT 270
Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys
85 90

CAG AAC GTT TTA AAT ACT CCG TTG ACT TTC 300
Gln Asn Val Leu Asn Thr Pro Leu Thr Phe
95 100

GGA CAG GGT ACC AAG GTG GAA ATA AAA CGT 330
Gly Gln Gly Thr Lys Val Glu Ile Lys Arg
105 110

ACT GGC GGT GGT GGT TCT GGT GGC GGT GCA 360
Thr Gly Gly Gly Gly Ser Gly Gly Gly Gly
115 120

TCT GGT GGT GGC GGT TCT CAA GTC CAA CTG 390
Ser Gly Gly Gly Gly Ser Gln Val Gln Leu
125 130

GTG CAA TCC GGC GCC GAG GTC AAG AAG CCA 420
Val Gln Ser Gly Ala Glu Val Lys Lys Pro
135 140

GGG GCC TCA GTC AAA GTG TCC TGT AAA GCT 450
Gly Ala Ser Val Lys Val Ser Cys Lys Ala
145 150

AGC GGC TAT ATT TTT TCT AAT TAT TGG ATT 480
Ser Gly Tyr Ile Phe Ser Asn Tyr Trp Ile
155 160

CAA TGG GTG CGT CAG GCC CCC GGG CAG GGC 510
Gln Trp Val Arg Gln Ala Pro Gly Gln Gly
165 170

WO 95/29697

2189015

PCT/US95/05688

- 140 -

CTG GAA TGG ATG GGT GAG ATC TTA CCG GGC 540
Leu Glu Trp Met Gly Glu Ile Leu Pro Gly
175 180

TCT GGT AGC ACC GAA TAT GCC CAA AAA TTC 570
Ser Gly Ser Thr Glu Tyr Ala Gln Lys Phe
185 190

CAG GGC CGT GTT ACT ATG ACG CGT GAC ACT 600
Gln Gly Arg Val Thr Met Thr Arg Asp Thr
195 200

TCG ACT AGT ACA GTA TAC ATG GAG CTC TCC 630
Ser Thr Ser Thr Val Tyr Met Glu Leu Ser
205 210

AGC CTG CGA TCG GAG GAC ACG GCC GTC TAT 660
Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr
215 220

TAT TGC GCG CGT TAT TTT TTT GGT TCT AGC 690
Tyr Cys Ala Arg Tyr Phe Phe Gly Ser Ser
225 230

CCG AAT TGG TAT TTT GAT GTT TGG GGT CAA 720
Pro Asn Trp Tyr Phe Asp Val Trp Gly Gln
235 240

GGA ACC CTG GTC ACT GTC TCG AGC TGA 747
Gly Thr Leu Val Thr Val Ser Ser
245

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5248 base pairs
- (B) TYPE: Nucleic Acid
- (C) STRANDEDNESS: Double

(D) TOPOLOGY: Circular
(ii) MOLECULE TYPE: Other nucleic acid
(A) DESCRIPTION: pET Trc S05/NI
prokaryotic expression vector

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

TGGCGAATGG GACGCGCCCT GTAGCGCGC ATTAAGCGCG GCGGGTGTGG 50
TGGTTACGCG CAGCGTGACC GCTACACTTG CCAGCGCCCT AGCGCCCGCT 100
CCTTCGCTT TCTCCCTTC CTTTCTCGCC ACGTTCGCGG GCTTTCCCGG 150
TCAAGCTCTA AATCGGGGGC TCCCTTTAGG GTTCGGATT AGTGCTTTAC 200
GGCACCTCGA CCCCAAAAAA CTTGATTAGG GTGATGGTTC ACGTAGTGGG 250
CCATCGCCCT GATAGACGGT TTTTCGCCCT TTGACGTGG AGTCCACGTT 300
CTTTAATAGT GGA CTCTTGT TCCAACTGG AACAACTC AACCTATCT 350
CGGTCTATTC TTTTGATTTA TAAGGGATT TGCCGATTTC GGCCTATTGG 400
TTAAAAAATG AGCTGATTTA AAAAAATTT AACGCGAATT TTAACAAAAT 450
ATTAACGTTT ACAATTTT CAG GTGGCACTTT TCGGGGAAAT GTGCGCGGAA 500
CCCCTATTTG TTTATTTTTC TAAATACATT CAATATGTA TCCGCTCATG 550
AGACAATAAC CCTGATAAAT GCTTCAATAA TATTGAAAAA GGAAGAGTAT 600
GAGTATTCAA CATTTCCGTG TCGCCCTTAT TCCCTTTTTT GCGGCATTTT 650
GCCTTCCTGT TTTTGCTCAC CCAGAAACGC TGGTGAAAGT AAAAGATGCT 700
GAAGATCAGT TGGGTGCACG AGTGGGTAC ATCGAACTGG ATCTCAACAG 750

CGGTAAGATC CTTGAGAGTT TTCGCCCCGA AGAACGTTTT CCAATGATGA ..800
GCACTTTTAA AGTTCTGCTA TGTGGCGCGG TATTATCCCG TATTGACGCC..850
GGGCAAGAGC AACTCGGTCG CCGCATACAC TATTCTCAGA ATGACTTGGT . 900
TGAGTACTCA CCAGTCACAG AAAAGCATCT TACGGATGGC ATGACAGTAA ..950
GAGAATTATG CAGTGTGCTC ATAACCATGA GTGATAACAC TGCGGCCAAC ..1000
TTACTTCTGA CAACGATCGG AGGACCGAAG GAGCTAACCG CTTTTTGA ..1050
CAACATGGGG GATCATGTAA CTCGCCCTGA TCGTTGGGAA CCGGAGCTGA ..1100
ATGAAGCCAT ACCAAACGAC GAGCGTGACA CCACGATGCC TGCAGCAATG ..1150
GCAACAACGT TGCGCAAACT ATTAACCTGGC GAACTACTTA CTCTAGCTTC ..1200
CCGGCAACAA TTAATAGACT GGATGGAGGC GGATAAGTT GCAGGACCAC ..1250
TTCTGCGCTC GGCCCTCCG GCTGGCTGGT TTATTGCTGA TAAATCTGGA ..1300
GCCGGTGAGC GTGGGTCTCG CGGTATCATT GCAGCACTGG GGCAGATGG ..1350
TAAGCCCTCC CGTATCGTAG TTATCTACAC GACGGGGAGT CAGGCAACTA ..1400
TGGATGAACG AAATAGACAG ATCGCTGAGA TAGGTGCCTC ACTGATTAAG ..1450
CATTGGTAAC TGTGAGACCA AGTTTACTCA TATATACTTT AGATTGATTT ..1500
AAACTTCAT TTTTAATTIA AAAGGATCTA GGTGAAGATC CTTTTTGATA ..1550
ATCTCATGAC CAAAATCCCT TAACGTGAGT TTTCGTTCCA CTGAGCGTCA ..1600
GACCCCGTAG AAAAGATCAA AGGATCTTCT TGAGATCCTT TTTTCTGCG ..1650
CGTAATCTGC TGCTTGCAAA CAAAAAACC ACCGCTACCA GCGGTGGTTT ..1700

2189015

GTTTGCCCGA TCAAGAGCTA CCAACTCTTT TTCCGAAGGT AACTGGCTTC 1750
AGCAGAGCGC AGATACCAA TACTGTCCTT CTAGGTAGC CGTAGTTAGG 1800
CCACCACTTC AAGAACTCTG TAGCACCGCC TACATACCTC GCTCTGCTAA 1850
TCCTGTTACC AGTGGCTGCT GCCAGTGGCG ATAAGTCGTG TCTTACCGGG 1900
TTGGA CTCAA GACGATAGTT ACCGGATAAG GCGCAGCGGT CGGGCTGAAC 1950
GGGGGGTTCG TGCACACAGC CCAGCTTGA GCGAACGACC TACACCGAAC 2000
TGAGATACCT ACAGCGTGAG CTATGAGAAA GCGCCACGCT TCCCGAAGGG 2050
AGAAAGGCGG ACAGGTATCC GGTAAAGCGG AGGGTCGGAA CAGGAGAGCG 2100
CAGGAGGGAG CTTCCAGGGG GAAACGCCTG GTATCTTTAT AGTCCTGTCG 2150
GGTTTCGCCA CCTCTGACTT GAGCGTCGAT TTTGTGATG CTCGTCAGGG 2200
GGGCGGAGCC TATGGAAAAA CGCCAGCAAC GCGGCCTTTT TACGGTTCTT 2250
GGCCTTTTGC TGGCCTTTTG CTCACATGTT CTTTCCTGCG TTATCCCCTG 2300
ATTCTGTGGA TAACCGTATT ACCGCCCTTG AGTGAGCTGA TACCGCTCGC 2350
CGCAGCCGAA CGACCGAGCG CAGCGAGTCA GTGAGCGAGG AAGCGGAAGA 2400
GCGCCTGATG CGGTATTTTC TCCTTACGCA TCTGTGCGGT ATTTACACCC 2450
GCATATATGG TGCACCTCTCA GTACAATCTG CTCTGATGCC GCATAGTTAA 2500
GCCAGTATAC ACTCCGCTAT CGCTACGTGA CTGGGTCATG GCTGCGCCCC 2550
GACACCCGCC AACACCCGCT GACGCGCCCT GACGGGCTTG TCTGCTCCCG 2600
GCATCCGCTT ACAGACAAGC TGTGACCGTC TCCGGGAGCT GCATGTGTCA 2650

GAGGTTTTC A CGTCATCAC CGAAACGCGC GAGGCAGCTG CGGTAAAGCT 2700
CATCAGCGTG GTCGTGAAGC GATTCACAGA TGTCTGCCTG TTCATCCGCG 2750
TCCAGCTCGT TGAGTTTCTC CAGAAGCGTT AATGTCIGGC TTCTGATAAA 2800
GCGGGCCATG TTAAGGGCGG TTTTTCCTG TTGGTCACT GATGCCTCCG 2850
TGTAAGGGG ATTTCTGTTC ATGGGGGTAA TGATACCGAT GAAACGAGAG 2900
AGGATGCTCA CGATACGGGT TACTGATGAT GAACATGCCC GGTACTGGA 2950
ACGTTGTGAG GGTAAACAAC TGCCGGTATG GATCGGCGG GACCAGAGAA 3000
AAATCACTCA GGGTCAATGC CAGCGCTTCG TTAATACAGA TGTAGGTGTT 3050
CCACAGGTA GCCAGCAGCA TCCTGCGATG CAGATCCGA ACATAATGTT 3100
GCAGGGCGCT GACTTCCGCG TTCCAGACT TTACGAAACA CGGAAACCGA 3150
AGACCATCA TGTGTGCT CAGGTGCGAG ACGTTTGCA GCAGAGTCG 3200
CTTCACGTT GCTCGGTAT CGGTGATTCA TTCTGCTAAC CAGTAAGCA 3250
ACCCCGCCAG CCTAGCCGGG TCCTCAACGA CAGGAGCAG ATCATGCGCA 3300
CCCGTGGGGC CGCCATGCCG GCGATAATGG CCTGCTTCTC GCCGAAACGT 3350
TTGGTGGCGG GACCAGTGAC GAAGGCTGA GCGAGGGCGT GCAAGATTCC 3400
GAATACCGCA AGCGACAGGC CGATCATCGT CGCGCTCCAG CGAAAGCGGT 3450
CCTCGCCGAA AATGACCCAG AGCGCTGCCG GCACCTGTCC TACGAGTGC 3500
ATGATAAAGA AGACAGTCAT AAGTGCGCG ACGATAGTCA TGCCCCGCGC 3550
CCACCGGAAG GAGCTGACTG GGTGAAGGC TCTCAAGGC ATCGGTGAG 3600

ATCCCGGTGC CTAATGAGTG AGCTAACTTA CATTAAATTGC GTTCGCTCA 3650
CTGCCCCGCTT TCCAGTCGGG AAACCTGTCG TGCCAGCTGC ATTAATGAAT 3700
CGGCCAACGC GCGGGGAGAG GCGGTTGCG TATTGGGCGC CAGGGTGGTT 3750
TTTCTTTTCA CCACTGAGAC GGGCAACAGC TGATTGCCCT TCACCGCCTG 3800
GCCCTGAGAG AGTTGCAGCA AGCGGTCCAC GCTGGTTTGC CCCAGCAGGC 3850
GAAAATCCTG TTTGATGGTG GTTAACGGCG GGATATAACA TGAGCTGTCT 3900
TCGGTATCGT CGTATCCCAC TACCGAGATA TCCGCACCAA CGCGCAGCCC 3950
GGACTCGGTA ATGGCGCGCA TTGCGCCAG CGCCATCTGA TCGTTGGCAA 4000
CCAGCATCGC AGTGGGAACG ATGCCCTCAT TCAGCATTTG CATGGTTTGT 4050
TGAAAACCGG ACATGGCACT CCACTCGCCT TCCCGTTCCG CTATCGGCTG 4100
AATTTGATTG CGAGTGAGAT ATTTATGCCA GCCAGCCAGA CGCAGACGCG 4150
CCGAGACAGA ACTTAATGGG CCCGCTAACA GCGCGATTG CTGGTGACCC 4200
AATGCGACCA GATGCTCCAC GCCCAGTCGC GTACCGTCTT CATGGGAGAA 4250
AATAATACTG TTGATGGGTG TCTGGTCAGA GACATCAAGA AATAACGCCG 4300
GAACATTAGT GCAGGCAGCT TCCACAGCAA TGGCATCCTG GTCATCCAGC 4350
GGATAGTTAA TGATCAGCCC ACTGACGCGT TGCCGAGAGAA GATTGTGCAC 4400
CGCCGCTTIA CAGGCTTCGA CGCCGCTTCG TTCTACCATC GACACCACCA 4450
CGCTGGCACC CAGTTGATCG GCGCGAGATT TAATCGCCGC GACAATTGTC 4500
GACGGCGCGT GCAGGGCCAG ACTGGAGGTG GCAACGCCAA TCAGCAACGA 4550

- 146 -

CTGTTTGCCC GCCAGTTGTT GTGCCACGCG GTTGGGAATG TAATTCAGCT 4600
CCGCCATCGC CGCTTCCACT TTTTCCCGCG TTTTCGCAGA AACGTGGCTG 4650
GCCTGGTTCA CCACGCGGGA AACGGTCTGA TAAGAGACAC CGGCATACTC 4700
TGCGACATCG TATAACGTTA CTGGTTTCAC ATTCACCACC CTGAATTGAC 4750
TCTCTTCCGG GCGCTATCAT GCCATACCGC GAAAGGTTTT GCGCCATTCT 4800
ATGGTGTCGG GGATCTCGAC GCTCTCCCTT ATGCGACTCC TGCATTAGGA 4850
AGCAGCCCAG TAGTAGGTTG AGGCCGTTGA GCACCGCCGC CGCAAGGAAT 4900
GGTGTCATCG GTACCAGCTG TTGACAATTA ATCATCCGGC TCGTATAATA 4950
GTACTGTGTG GAATTGTGAG CGCTCACAAT TCCACACATC TAGAAATAAT 5000
TTTGTTTAAAC TTTAAGAAGG AGATATACCA TGGAGATCTG GATCCATCGA 5050
TGAATTCGAG CTCCGTCGAC AAGCTTGCGG CCGCACTCGA GCACCACCAC 5100
CACCACCACT GAGATCCGGC TGCTAACAAA GCCCGAAAGG AAGCTGAGTT 5150
GGCTGCTGCC ACCGCTGAGC AATAACTAGC ATAACCCCTT GGGGCCTCTA 5200
AACGGGTCTT GAGGGGTTTT TTGCTGAAAG GAGGAACTAT ATCCGGAT 5248

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 813 base pairs
- (B) TYPE: Nucleic Acid
- (C) STRANDEDNESS: Double
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: Other nucleic acid

- (A) DESCRIPTION: N19/8 scFv (His Tagged)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

ATG GCC AAT ATT GTG CTG ACC CAA TCT CCA 30
Met Ala Asn Ile Val Leu Thr Gln Ser Pro
1 5 10

GCT TCT TTG GCT GTG TCT CTA GGG CAG AGG 60
Ala Ser Leu Ala Val Ser Leu Gly Gln Arg
15 20

GCC ACC ATA TCC TGC AGA GCC AGT GAA AGT 120
Ala Thr Ile Ser Cys Arg Ala Ser Glu Ser
25 30

GTT GAT AGT TAT GAC AAT AGT TTT ATG CAC 150
Val Asp Ser Tyr Asp Asn Ser Phe Met His
35 40

TGG TAC CAG CAG AAA CCA GGA CAG CCA CCC 180
Trp Tyr Gln Gln Lys Pro Gly Gln Pro Pro
45 50

AAA CTC CTC ATC TTT CTT GCA TCC AAC CTA 210
Lys Leu Leu Ile Phe Leu Ala Ser Asn Leu
55 60

GAA TCT GGG GTC CCT GCC AGG TTC AGT GGC 240
Glu Ser Gly Val Pro Ala Arg Phe Ser Gly
65 70

AGT GGG TCT AGG ACA GAC TTC ACC CTC ACC 270
Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr
75 80

ATT GAT CCT GTG GAG GCT GAT GAT GCT GCA 300
Ile Asp Pro Val Glu Ala Asp Asp Ala Ala
85 90

ACC TAT TAC TGT CAG CAA AAT AAT GAG GTT 330
Thr Tyr Tyr Cys Gln Gln Asn Asn Glu Val
95 100

CCG AAC ACG TTC GGA GGG GGG ACC AAG CTG 360
Pro Asn Thr Phe Gly Gly Gly Thr Lys Leu
105 110

GAA ATA AAA CGG ACC GGA GGT GGC GGG TCG 390
Glu Ile Lys Arg Thr Gly Gly Gly Gly Ser
115 120

GGT GGC GGG GGA TCG GGT GGC GGA GGG TCG 420
Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
125 130

GAC GTC AAG CTC GTG GAG TCT GGG GGA GAC 450
Asp Val Lys Leu Val Glu Ser Gly Gly Asp
135 140

TTA GTG AAG CTT GGA GGG TCC CTG AAA CTC 480
Leu Val Lys Leu Gly Gly Ser Leu Lys Leu
145 150

TCC TGT GCA GCC TCT GGA TTC ACC TTC AGT 510
Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser
155 160

AGC TAT TAT ATG TCT TGG GTT CGC CAG ATT 540
Ser Tyr Tyr Met Ser Trp Val Arg Gln Ile
165 170

TCA GAG AAG AGG CTG GAG TTG GTC GCA GCC 570
Ser Glu Lys Arg Leu Glu Leu Val Ala Ala
175 180

WO 95/29697

PCT/US95/05688

2189015

- 149 -

ATT AAT AGT AAT GGT GAT AGC ACC TAC TAT 600
Ile Asn Ser Asn Gly Asp Ser Thr Tyr Tyr
185 190

CCA GAC ACT GTG AAG GGC CGA TTC ACC ATC 630
Pro Asp Thr Val Lys Gly Arg Phe Thr Ile
195 200

TCC AGA GAC AAT GCC AAG AGC ACC CTG GAT 660
Ser Arg Asp Asn Ala Lys Ser Thr Leu Asp
205 210

CTG CAA ATG AGC AGT CTG AAG TCT GAG GAC 690
Leu Gln Met Ser Ser Leu Lys Ser Glu Asp
215 220

ACA GCC TTG TAT TTC TGT GTA AGA GAG ACT 720
Thr Ala Leu Tyr Phe Cys Val Arg Glu Thr
225 230

TAT TAC TAC GGG ATT AGT CCC GTC TTC GAT 750
Tyr Tyr Tyr Gly Ile Ser Pro Val Phe Asp
235 240

GTC TGG GGC ACA GGG ACC ACG GTC ACC GTC 780
Val Trp Gly Thr Gly Thr Thr Val Thr Val
245 250

TCC TCA CTC GAG CAC CAC CAC CAC CAC 810
Ser Ser Leu Glu His His His His His His
255 260

TGA 813

2189015

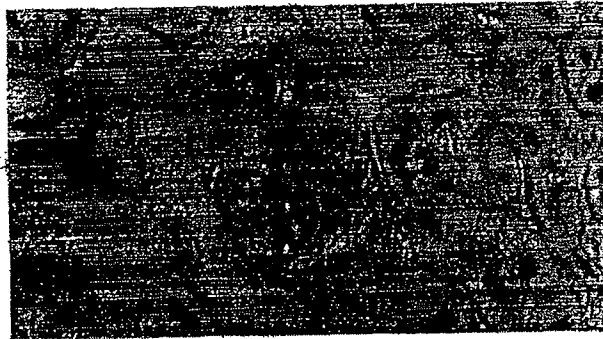


FIG. 1A

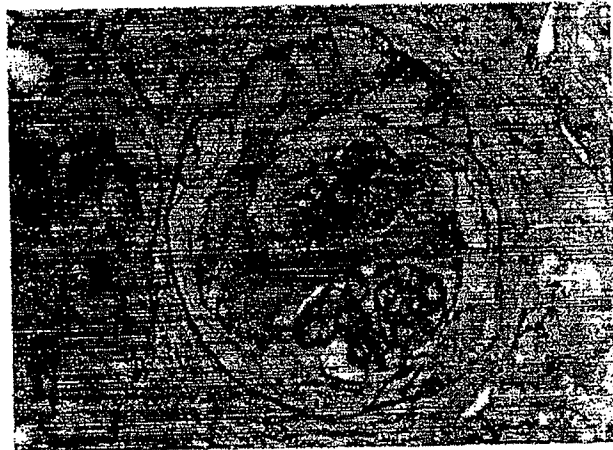


FIG. 1B



FIG. 1C

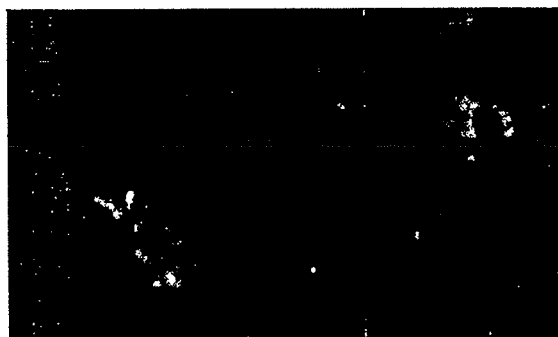


FIG. 2A



FIG. 2B



FIG. 2C

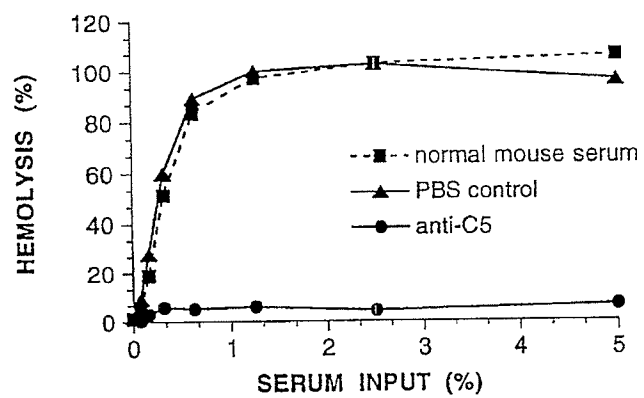


FIG. 3

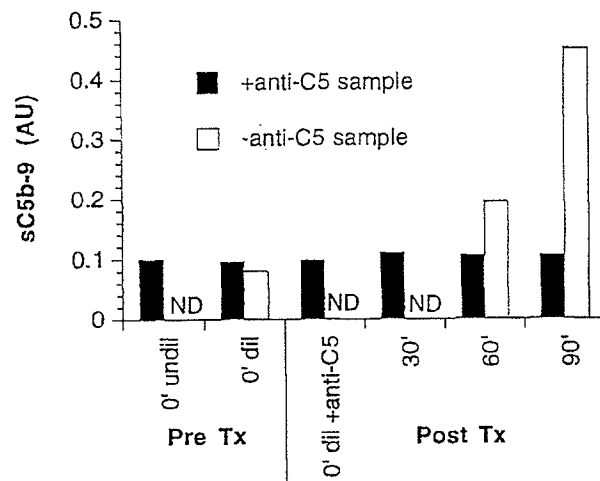
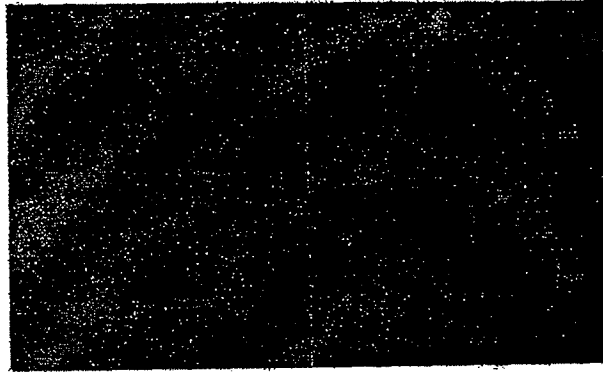


FIG. 4

SUBSTITUTE SHEET (RULE 26)

FIG. 5A



2189015

5 / 19 / 1

PCT/US95/05688

WO 95/29697

WO 95/29697

PCT/US95/05688

5 / 1 9 / 2

2189015



FIG. 5B

SUBSTITUTE SHEET (RULE 26)

WO 95/29697

PCT/US95/05688

5 / 1 9 / 3

2189015



FIG. 5C

SUBSTITUTE SHEET (RULE 26)

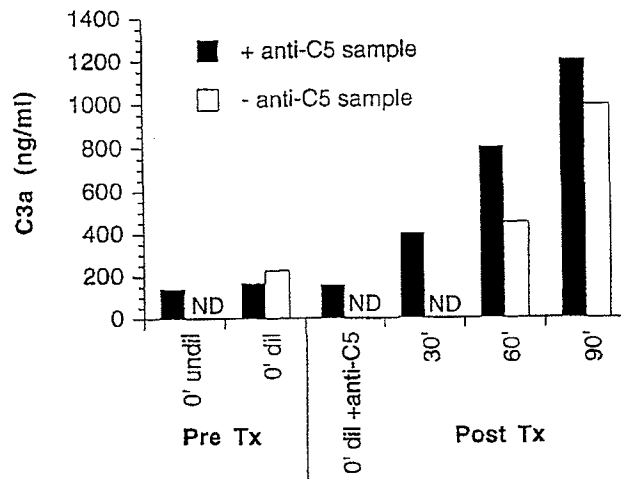


FIG. 6

7 / 19

2189015

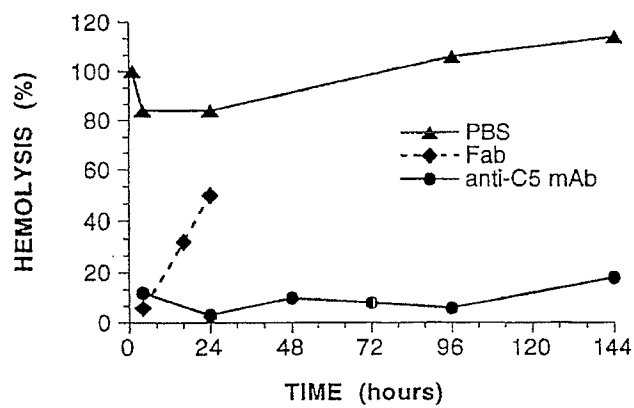


FIG. 7A

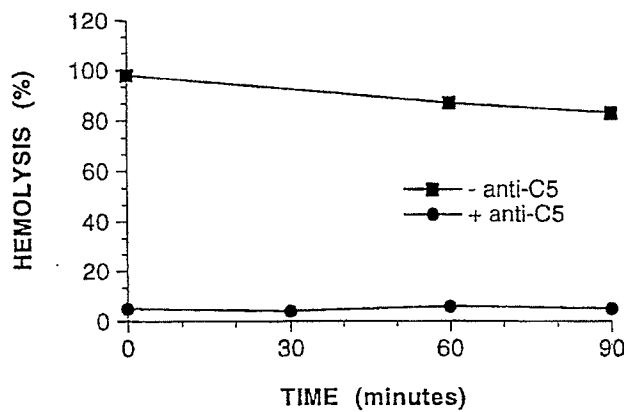


FIG. 7B

2189015

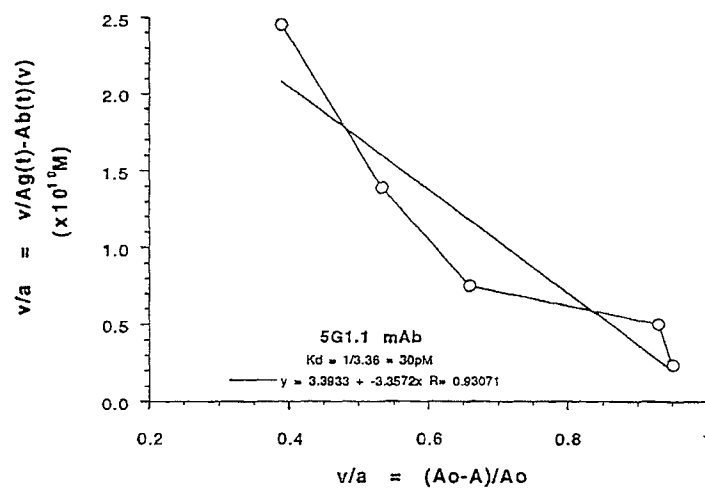


Fig. 8

2189015

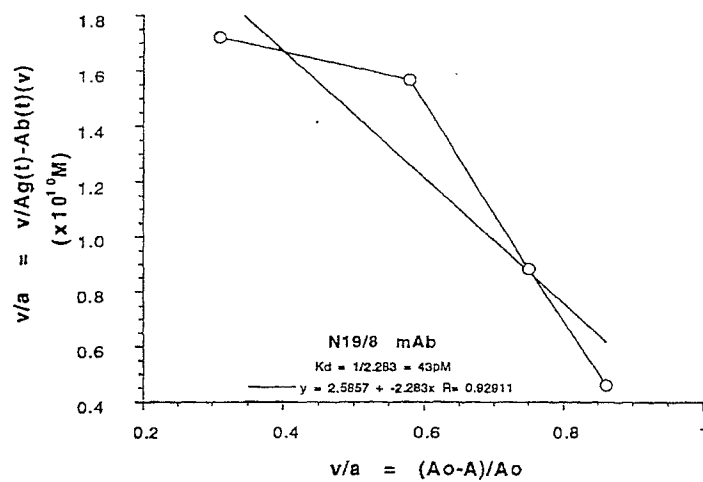


Fig. 9

10 / 19

2189015

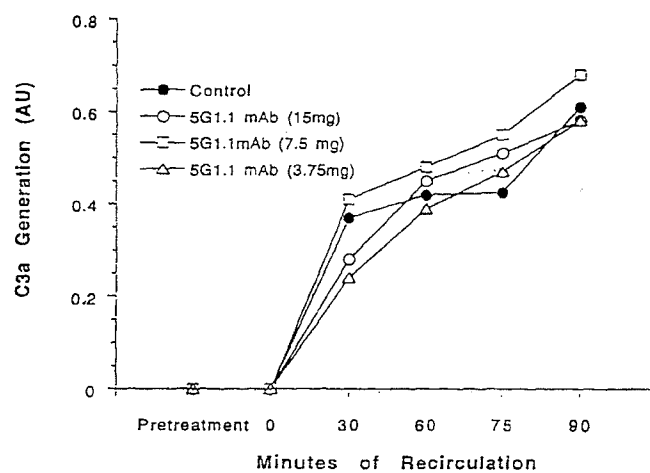


Fig. 10

11/19

2189015

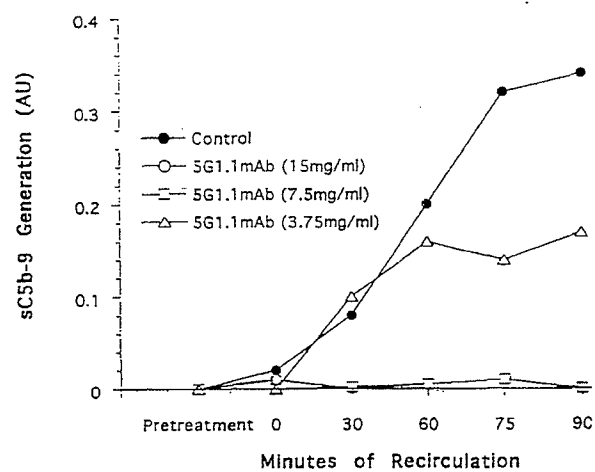


Fig. 11

12 / 19

2189015

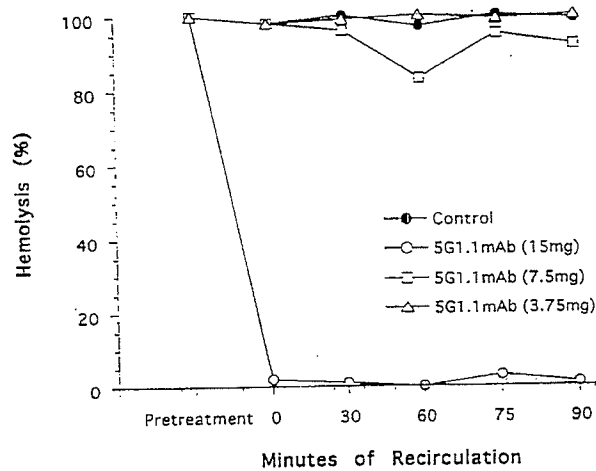


Fig. 12

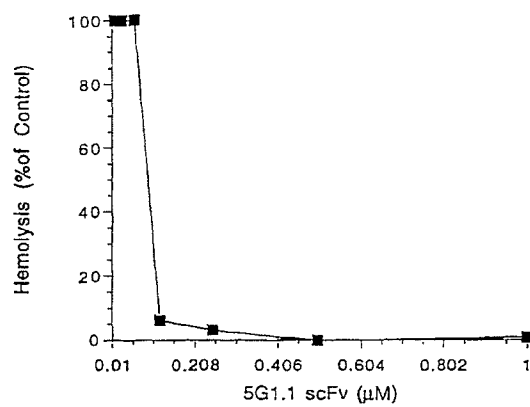


Fig. 13

2189015

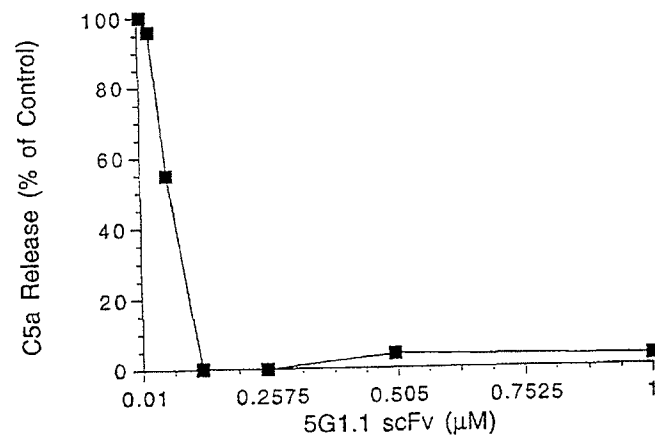


Fig. 14

2189015

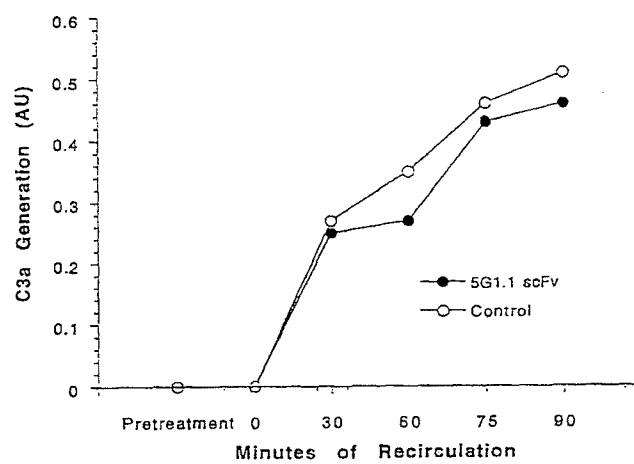


Fig. 15

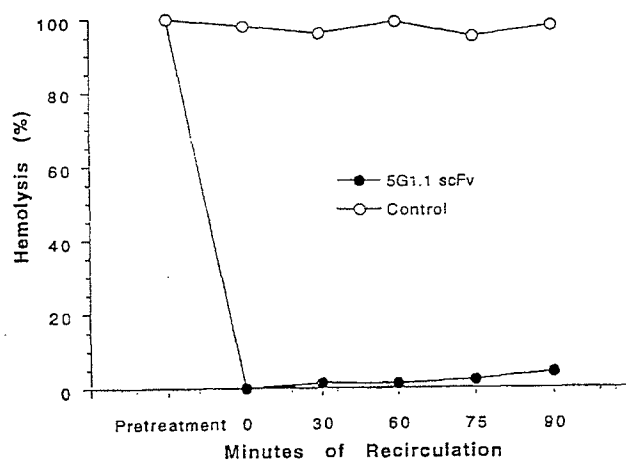


Fig. 16

2189015

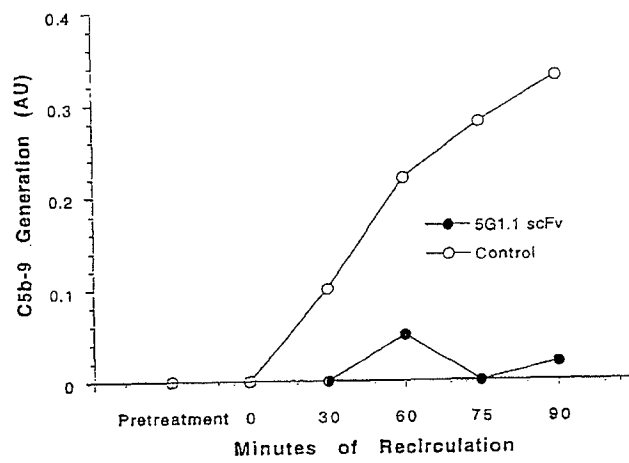


Fig. 17

2189015

Fig. 18

2189015

-19
atg aaa tgg agc tgg att att ctc ctc ctg tca gta act gca ggt gtc cac tcc cag
m k w s w v i l f l l s v t a g v h s q

-1 +1

ggt cag ctg cag cag tct oga gct gag ctg atg aag cct ggg gcc tca gta aag atg tcc
v o l o o s g a e l m k p g a s v k m s

10 20

26 30 35 40
tgc aag gct act gcc tgc atg ttc agt aac tgc atg cag tgg ata aag cag agc cct
c k a t g y i f s n y w i q
cdr-h1

50 52a 60
gga cat gcc ctt gag tgg att ggt gag att tta cct gaa agt ggt tct act gag tgc act
g h g l e w i g e i l p g s g s t e y t

70 80
gag aac ttc aag gac aag gcc gca ttc act gca gat aca tcc tcc aac aca gcc tgc atg
e n f k d k a a f t a d t s s n t a y m

82a 82b 82c 90
caa ctc agc agc ctg aca tca gag gac tct gcc gtc tat tgc tgc aca aga tat ttc ttc
q l s s l t s e d s a v y y c a r y f f

95 100 a b c d e 102
ggt agt agc ccc aac tgg tac ttc gat tgg ggc gca ggg acc acg gtc acc gtc tcc
g s s p n w y f d v w g a g t t v t v s

110
cdr-h3

tca
s

Fig. 19